UNITED STATES PATENT AND TRADEMARK OFFICE

UNITED STATES DEPARTMENT OF COMMERCE
United States Patent and Trademark Office
Address: COMMISSIONER FOR PATENTS
P.O. Box 1450
Alexandria, Virginia 22313-1450
www.uspto.gov

APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/678,756	10/02/2003	Mary Jo Ondrechen	NU-593XX	6620

207 7590 09/17/2007
WEINGARTEN, SCHURGIN, GAGNEBIN & LEBOVICI LLP
TEN POST OFFICE SQUARE
BOSTON, MA 02109

EXAMINER	
RIGGS II, LARRY D	
ART UNIT	**PAPER NUMBER**
1631	
MAIL DATE	**DELIVERY MODE**
09/17/2007	PAPER

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

PTOL-90A (Rev. 04/07)

Office Action Summary	**Application No.** 10/678,756	**Applicant(s)** ONDRECHEN ET AL.	
	Examiner Larry D. Riggs II	**Art Unit** 1631	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on 25 June 2007.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) 1-16 is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) 1-16 is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO/SB/08)
Paper No(s)/Mail Date _____.

4) ☐ Interview Summary (PTO-413)
Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

The instant application has been transferred to examiner Larry D. Riggs II in art unit 1631.

Declaration under 37 C.F.R. 1.132

The signed declaration of Mary Jo Ondrechen, filed 25 June 2007 has been considered.

Priority

In absence of the citation of intervening prior art the question of priority under 35 U.S.C 112 in the Office action mailed 22 March 2007 is withdrawn.

Specification

The objection to browser-executable code in the Office action mailed 22 March 2007 is withdrawn in view of the amendment to the specification, filed 25 June 2007.

Claim Rejections - 35 USC § 101

The rejection of claims 1-16 under 35 U.S.C. 101 in the Office action mailed 22 March 2007 is withdrawn in view of the amendment filed 25 June 2007.

Claim Rejections - 35 USC § 112, 1st Paragraph

The rejection of claims 1-3 and 6-16 under 35 U.S.C. 112 in the Office action mailed 22 March 2007 is withdrawn in view of the explanation of specification and examples, (see page 6, lines 12-31), filed 25 June 2007.

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 1-16 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for determining interaction sites in a protein of experimentally determined structures, does not reasonably provide enablement for determining interaction sites in protein structures not experimentally determined. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to use the invention commensurate in scope with these claims.

In *In re* Wands (8 USPQ2d 1400 (CAFC 1988)) the CAFC considered the issue of enablement in molecular biology. The CAFC summarized eight factors to be considered in a determination of "undue experimentation." These factors include: (a) the quantity of experimentation necessary; (b) the amount of direction or guidance presented; (c) the presence or absence of working examples; (d) the nature of the invention; (e) the state of the prior art; (f) the relative skill of those in the art; (g) the predictability of the art; and (h) the breadth of the claims.

In considering the factors for the instant claims:

a) In order to use the claimed invention one of skill in the art must obtain the interaction site, which requires a structure for the protein, but not require the structure be experimentally determined. For the reasons discussed below, there would be an unpredictable amount of experimentation required to practice the claimed invention.

b) The description describes that the protein does not have to bear any resemblance in sequence or structure to any previously characterized protein for the invention to be applicable and that a three-dimensional structure of the protein can be theoretically predicted using a modeling method, thereafter the method of the invention to the theoretical three-dimensional structure can be applied, (see specification page 6, lines 14-31). The description does not provide detailed guidance to obtain a theoretical three-dimensional structure without *ab initio* structure prediction to determine its structure.

c) The description provides working examples from experimentally determined protein structures. The description does not provide working examples of a truly novel protein with a structure not experimentally determined, for which an algorithm could make correct predictions.

d) The nature of the invention, predicting protein interaction sites, is complex.

e) The prior art does not show reliable prediction of a protein structure and the protein's interaction site from a primary sequence of the protein. Xu et al. (Current Protein and Peptide Science, Vol. 1, Pages 1-21, 2000) discloses that such prediction mechanisms are extremely difficult and are generally unreliable (for example, see page 15, 2nd column, 1st paragraph, lines 2-6). Furthermore, even if an overall structure could be obtained through homology modeling, Xu discloses that it would be difficult to obtain the structure of the interaction site if the interaction site residues were to lie in a region in which there was an extended gap relative to the protein sequence of the template structure (for example, see page 12, 2nd column, 2nd paragraph, lines 10-12).

f) The skill of those in the art of computational prediction of protein interaction and protein modeling is high.

g) The predictability of a reliable interaction site from a theoretical model structure of a novel protein is not described in the prior art.

h) The claims are broad in that they are drawn to any protein that does not bear any resemblance in sequence or structure to any previously characterized protein whose theoretical three-dimensional structure relationship to the protein's interactive site is not established.

The skilled practitioner would first turn to the instant description for guidance in using the claimed invention. However, the description lacks clear evidence of enabling the reliable prediction of a theoretical three-dimensional structure of a novel protein and prediction of the protein's interactive site. As such, the skilled practitioner would turn to the prior art for such guidance, however the prior art provides that such prediction mechanisms are extremely difficult and are generally unreliable. Finally, said practitioner would turn to trial and error experimentation to determine a reliable prediction of a theoretical three-dimensional structure of a novel protein. Such amounts to undue experimentation.

Claim 5 is rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention. This rejection is newly applied.

The claims are drawn to a method for determining a putative interaction site in a protein requiring the ability to obtain a structure of the protein.

In analysis of claims for compliance with the written description requirement of 35 U.S.C. 112, first paragraph, regarding genus/species situations, the written description guidelines note that "satisfactory disclosure of a 'representative number' depends on whether one of skill in the art would recognize that the applicant was in possession of the necessary common attributes or features of the elements possessed by the members of the genus in view of the species disclosed." (See: Federal Register: December 21, 1999 (Volume 64, Number 244), revised guidelines for written description, which can be obtained from the US PTO website: <http://www.uspto.gov>). Given that the genus essentially includes obtaining the interaction site which requires a structure for the protein but not requiring the structure be experimentally determined, one of ordinary skill in the art would have reasonable doubt applicant had possession of the claimed genus at the time the application was filed. Despite applicant's assertion that proteins examined using the claimed invention "does not have to bear any resemblance in sequence or structure to any previously characterized protein" (specification, page 6, lines 14-16), a truly novel protein with no relatedness to a experimentally determined protein or structure would require *ab initio* structure prediction to determine its structure. Xu et al. (Current Protein and Peptide Science, Vol. 1, Pages 1-21, 2000) discloses that such prediction mechanisms are extremely difficult and are generally unreliable (for example, see page 15, 2nd column, 1st paragraph, lines 2-6). Furthermore, even if an overall structure could be obtained through homology modeling, Xu discloses that it would be difficult to obtain the structure of the interaction site if the interaction site residues were to lie in a region in which there was an extended gap relative to the protein sequence of the template structure (for example, see page 12, 2nd column, 2nd paragraph, lines 10-12). Given the limitations of the protein arts, applicant's admission that poor quality structures can lead to problems in predicting interaction residues (for example, page 17, lines 11-16), and the fact that applicant hasn't provided any examples of a truly novel protein with a structure that has not been experimentally determined, for which the algorithm makes correct predictions, one of ordinary skill in the art would have considerable doubt that applicant had possession of the claimed genus at the time the application was filed.

Response to Arguments

Applicant's arguments filed 25 June 2007 have been fully considered and are persuasive only in part. Applicant's point out that the protein structure can be "downloaded from a database" or "determined experimentally", or determined as "theoretical model structure". Two options provide the ability of one skilled in the art to obtain an experimentally determined protein structure and use the instant invention, as in claims 1-3 and 6-16. However, given the limitations of the art, the Applicant's admitted limitation of the invention of predicting interaction residues with a truly novel protein and lack of examples with a protein structure that has not been experimentally determined, one of ordinary skill in the art would have considerable doubt that applicant had possession of the claimed genus at the time the application was filed.

Claim Rejections - 35 USC § 112, 2nd Paragraph

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claim 4 is rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claim 4 recites the limitation "structure of said protein in known" in line 2. It is unclear who knew the protein structure or when they knew it. Did the public, the inventor or persons investigating the protein structure know of the structure? Was the protein structure known at the time of filing, the day the data for the protein structure was obtained, or the day the invention was published? Applicant is urged to delete the term “known” in line 2 of the instant claim.

Claim Rejections - 35 USC § 102

The rejection of claims 1-4, 6 and 11-16 under 35 U.S.C. 102 in the Office action mailed 22 March 2007 is withdrawn in view of the declaration filed 25 June 2007.

Claim Rejections - 35 USC § 103

The rejection of claim 5 under 35 U.S.C. 103 in the Office action mailed 22 March 2007 is withdrawn in view of the declaration filed 25 June 2007.

Conclusion

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Larry D. Riggs II whose telephone number is 571-270-3062. The examiner can normally be reached on Monday-Thursday, 7:30AM-5:00PM, ALT. Friday, EST.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Marjorie Moran can be reached on 571-272-0720. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

/LDR/
Larry D. Riggs II
Examiner, Art Unit 1631

/John S. Brusca/
Primary Examiner
Art Unit 1631